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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,451	10/04/2005	Frank Giles	ON/4-32719A	3037
1095	7590	01/17/2008		
NOVARTIS CORPORATE INTELLECTUAL PROPERTY ONE HEALTH PLAZA 104/3 EAST HANOVER, NJ 07936-1080			EXAMINER TEALE, MICHAEL J	
			ART UNIT	PAPER NUMBER
			1611	
			MAIL DATE	DELIVERY MODE
			01/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,451	GILES, FRANK	
	Examiner	Art Unit	
	Michael J. Teale Ph.D.	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 December 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) 6-14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>05/17/2006</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's election without traverse of Group I claims 1-5 in the reply filed on 12/05/2007 is acknowledged. Election of PTK787 (1-[4-chloroanilino]-4-[4-pyridylmethyl]), is also acknowledged, and for the record, applicant's election appears to read on claims 1-5. Claims 6-14 are withdrawn along with the remaining compounds as claimed from further consideration pursuant 37 CFR 1.142(b), to as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Applicant is advised that the restriction is made **Final**.

The Information Disclosure Statement filed May 17, 2006 is acknowledged. Applicant is advised that several references were not included in the filing.

2. ***Claim Rejection - 35 USC § 112, First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for treating agnogenic myeloid metaplasia (AMM) in a warm-blooded animal or human by administering PTK787. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988). These factors include:

- 1) the nature of the invention;
- 2) the breadth of the claims;
- 3) the predictability or unpredictability of the art;
- 4) the amount of direction or guidance presented;
- 5) the presence or absence of working examples;
- 6) the quantity of experimentation necessary;
- 7) the state of the prior art; and,
- 8) the relative skill of those skilled in the art.

The relevant factors are addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

Factors 1 and 2) The claimed invention is directed to a method for treating agnogenic myeloid metaplasia (AMM) in a warm-blooded animal or human by administering PTK787 (claims 1-5).

Factor 5) The instant specification examples (pages 9 and 10 of the specification as filed) disclose two patients, one with the symptom of splenomegaly (a condition well known in the art), and the other with a protuberant spleen where the cause(s) of said conditions are not disclosed. It is reported administration of PTK787 gave the patients some relief from their symptoms. While this result may be enabling for treating enlarged spleens it says nothing about treating AMM, where an enlarged spleen may be due to a number of unrelated underlying causes. Barosi (*J. of Clin. Onco.*, Vol. 17:2954-2970, 1999) teaches that there are a number of symptoms common to AMM (page 2958, see DISEASE FEATURES) and while splenomegaly may be one of them (however not with childhood onset), it is not the only major symptom. Since

splenomegaly taken by itself may be due to other causes, it is clear that this symptom alone is not sufficient to be predictive of AMM.

Summary

The applicant has not established that AMM was in fact the cause of the symptoms of the patients treated with the proposed invention in the examples disclosed. As the cited art and discussion of the above factors establish, practicing the claimed method in the manner disclosed by Applicant would not imbue the skilled artisan with a reasonable expectation that PTK787 would be effective in treating AMM. It is clear from the discussion above that the skilled artisan could not rely on Applicant's disclosure as required by 35 U.S.C. §112, first paragraph. Given that the applicant has failed to demonstrate that warm-blooded animals and/or humans with AMM could be efficaciously treated by the administration of PTK787, the skilled artisan would be faced with the impermissible burden of undue experimentation in order to practice this embodiment of the claimed invention. Accordingly, claims 1-5 are rejected.

Claim Rejection - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tille *et al.*, (*JPET* vol. 299:1073-1085, 2001), in view of Barosi (*J. of Clin. Onco.* Vol. 17:2954-2970, 1999).

The instant application claims are drawn to a method for treating agnogenic myeloid metaplasia (AMM) in a warm-blooded animal and/or a human by administering PTK787 (claims 1-5).

Tille teaches that PTK787 is an effective inhibitor of b-FGF (Abstract:1073, Results: page 1076) and .

Tille does not teach that PTK787 may be used to treat AMM.

Barosi teaches that deregulation of the b-FGF pathway in primitive hematopoietic stem cells is hypothesized to be a primary event in the abnormal hematopoiesis of MMM (also known as AMM) (page 2955, Myeloid Proliferative Advantage, col. 2, paragraph 2). It would have been reasonable to expect that inhibition of this pathway would be a treatment for AMM.

Since Tille teaches PTK787 inhibits the b-FGF pathway and Barosi suggests b-FGF pathway inhibition would likely be a treatment for AMM, it would have been obvious for some one of ordinary skill in the art to administer PTK787 as a b-FGF inhibitor to treat AMM.

No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael J. Teale Ph.D. whose telephone number is (571)-272-6897. The examiner can normally be reached on 7:30 am to 4:30 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571)-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



MJT



1/14/08

PHYLLIS SPIVACK
PRIMARY EXAMINER